ALUMINUM TOXICITY*

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IT has been assumed that the lung, skin, and gastrointestinal tract are largely impervious barriers to aluminum, preventing the accumulation of this element in the body. However, it is now apparent in certain pathological states that the body burden of aluminum may be markedly increased with resulting toxicity.

There is little evidence that aluminum is an essential element for either animals or plants. The body burden of this element normally in most tissues is less than 4 mg/kg dry weight and the total body burden is less than 50 mg.[1] Although aluminum comprises 5% of the earth's crust and is ubiquitous, it would appear that only 2 to 3 mg are ingested daily as a contaminant in food sources.[2] Only a small fraction of ingested aluminum is absorbed. This absorbed aluminum is largely eliminated from the body by the kidney, and urinary aluminum averages 10 to 15 μg/day.[3] When the amount of ingested aluminum is markedly increased, urinary aluminum may increase by 20- to 40-fold to 200 to 500 μg/day. However, even under these conditions there is little evidence that any aluminum is retained in the body. If, however, renal function is impaired, ability to excrete absorbed aluminum may be markedly compromised and the body burden of aluminum increased. This is supported by the increased aluminum concentrations found in approximately 80% of nondialyzed uremic patients.[4]

The second mechanism which may enhance the body burden of aluminum is parenteral administration of aluminum. This was first recognized in dialyzed uremic patients receiving chronic dialysis with aluminum-contaminated dialysate. This contamination resulted from tap water used to prepare the dialysate. Usually, the increased tap water aluminum resulted from water treatment where aluminum sulfate was used as a coagulum. It was found that as much as 1 to 2 mg of aluminum could be

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transferred to the patient during the course of a single dialysis from this source.[5] Most of this aluminum appeared to be retained by the patient, since such patients had virtually no renal function and were unable to excrete the administered aluminum.

However, even individuals with normal renal function, when given large parenteral loads of aluminum, are unable fully to eliminate the administered aluminum. It was found that patients receiving total parenteral nutrition with casein hydrolysate serving as the amino acid source were given 2 to 3 mg of aluminum daily intravenously as a result of aluminum contamination of the casein.[6] Balance studies in three patients undergoing this therapy showed a mean daily aluminum infusion of 1,709 μg, urinary aluminum excretion of 882 μg, and fecal aluminum excretion of 34 μg/day, which represented a daily net retention of 793 μg/day. Retention of aluminum was further documented by a mean liver aluminum concentration of 84 $\pm$ 21 mg/kg (normal $<$ 6) and bone aluminum content ranging between 14 and 265 mg/kg (normal $<$ 10) in these patients.[7]

Increasing evidence suggests that this retained aluminum is associated with systemic toxicity. In 1976 it was first suggested that dialysis encephalopathy, previously a uniformly fatal neurological syndrome, resulted from aluminum intoxication.[8] Based on additional biochemical and epidemiological data, this supposition was confirmed and now it is generally accepted that aluminum is indeed the cause of this syndrome.[9,10]

In 1978 epidemiological surveys revealed a high association between dialysis encephalopathy and a disabling form of osteomalacia in dialysis patients, suggesting that this latter disease also resulted from aluminum intoxication.[11,12] Additional support for this contention came from animal studies where osteomalacia could be induced in rats by large parenteral loads of aluminum.[13] It was subsequently shown that dialysis patients with osteomalacia had significantly higher bone aluminum levels than dialysis patients with other forms of bone disease and that the aluminum levels correlated directly with the amount of uncalcified osteoid in the bone section.[14]

Based on these observations, it has been suggested that aluminum may play a role in the pathogenesis of osteomalacia related to total parenteral nutrition. In this population as well, bone aluminum levels correlated inversely with bone formation rates ($r = 0.76$).[7] There are other similarities between the osteomalacia occurring in these patients and that associated with aluminum in uremic patients. Beside the histological features in both groups of patients, $1,25(OH)_2D_3$ levels and parathyroid hormone

levels are low.[15]

In conclusion, it is now well established that under certain conditions—loss of renal function and the parenteral administration of aluminum—the body burden of aluminum may be markedly increased. The evidence is also strong that this enhanced body burden of aluminum may be accompanied by systemic toxicity.

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